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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,862	12/15/2005	Leifeng Cheng	101079-1P US	2351

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EXAMINER	
JAISLE, CECILIA M	
ART UNIT	**PAPER NUMBER**
1624	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,862	CHENG, LEIFENG	
	Examiner	Art Unit	
	Cecilia M. Jaisle	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8 and 10-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8 and 10-14* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09-08-2008 & 01-22-2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application on Sept. 8, 2008 after issuance of a Notice of Allowance, issued June 9, 2008. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on Sept. 8, 2008 has been entered.

Information Disclosure Statement

Applicants are requested to explain the significance of US Pat. No. 5145648, issued 06-02-1992, entitled Exhaust Smoke Purifier Apparatus. If this document was cited in error, Applicants are requested to cite the correctly intended document.

Rejections Under 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification to enable one skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention. The specification does not reasonably enable treatment of obesity (claim 10 and 11), extended abuse, addiction and/or relapse indications (claim 10).

The specification asserts the claimed compounds are CB1 (cannabinoid receptor type 1) modulators and therefor of value in the above recited conditions, for which insufficient enablement is provided. Substantiation of utility and its scope is required when utility is "speculative," "sufficiently unusual" or not provided. See *Ex parte Jovanovics, et al.*, 211 USPQ 907, 909 (BPAI 1981). *Hoffman v. Klaus*, 9 USPQ2d 1657 (BPAI 1988) and *Ex parte Powers*, 220 USPQ 924 (BPAI 1982) regarding types of testing needed to support *in vivo* uses.

Applicants' attention is drawn to the Revised Interim Utility and Written Description Guidelines, 66 FR 1092-1099 (2001), emphasizing "a claimed invention must have a specific and substantial utility." MPEP 2163, *et. seq*. This disclosure is insufficient to enable the claimed methods based on the disclosed PDE2 inhibition.

MPEP § 2164.01(a) states:

> A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Many factors require consideration when determining whether sufficient evidence supports a conclusion that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue." MPEP 2164.01(a). These factors include: (1) the claim breadth; (2) the nature of the invention; (3) the state of the prior

art; (4) the level of predictability in the art; (5) the amount of direction provided by the inventor; (6) the presence of working examples; and (7) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)(reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement). See also *In re Goodman* 29 USPQ2d 2010, 2013 (Fed. Cir. 1993). Application of these factors to the present application supports the determination that the present disclosure fails to satisfy the enablement requirement:

1. **Breadth of the claim:**

(a) Scope of the methods. The claims cover methods using substituted 5,6-diaryl-pyrazine-2-carboxamides and -2-sulfonamides related compounds.

(b) Scope of the conditions covered. The claims cover methods to treat above conditions said to be responsive to CB1 modulators.

- The goal of **obesity treatment** is to achieve and maintain a healthier weight. Achieving a healthy weight usually requires a combination of dietary changes, increased activity and behavior modification. Depending on the individual situation, medication or weight-loss surgery may supplement these efforts.

- It is not possible to determine what is intended by **treatment of extended abuse, addiction and/or relapse indications**. **Abuse** may refer to physical, substance or sexual abuse, all of which require extremely different treatment forms. The term "**addiction"** is used in many contexts to describe any obsession, compulsion, or excessive or psychological dependence, e.g., drug

addiction, crime, alcohol, tobacco, compulsive overeating, sex, problem gambling, computer addiction, pornography, etc. **Relapse indications** include return of disease signs and symptoms after a patient has enjoyed remission. For example, after treatment a patient with colon cancer went into remission with no sign or symptom of the tumor, remained in remission for years, but then suffered a relapse and had to be treated once again for colon cancer.

The specification fails to identify treatment results with methods of this invention and how to recognize such results. Each of the above conditions has various symptoms and there is no indication of which specific symptoms are treated.

2. **Nature of the invention and predictability in the art:** The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970).

Pharmacological activity in general is unpredictable. In applications involving physiological activity, such as the present:

> The first paragraph of 35 U.S.C. §112 effectively requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.

Plant Genetic Systems v. DeKalb Genetics Corp., 65 USPQ2d 1452 (CAFC 2003).

3. **Direction and Guidance:** That provided is very limited. The dosage range information is meager at best. It is generic, the same for all disorders the

specification covers. No specific direction or guidance provides a regimen or dosage effective specifically for all of the conditions construed by the claim.

4. **State of the prior art:** The art indicates the need for undue experimentation.

Koroneos, PharmExec.com, Nov. 12, 2008, <http://pharmexec.findpharma.com/pharmexec/News/CB-1-Antagonists-for-Obesity-RIP/ArticleStandard/Article/detail/565272?contextCategoryId=43778>, downloaded 1/22/2009, disappointingly reported:

> Last week, Pfizer and Sanofi-Aventis announced that they had ended all clinical trials for their CB-1 antagonist obesity treatments. The drugs target the cannabinoid type 1 receptor in the brain, basically turning off the pleasure center that causes people to crave food. Both Pfizer's Phase III drug CP-945,598 and Sanofi-Aventis's Acomplia (rimonabant) had been universally criticized for causing psychiatric adverse reactions in patients using the drugs.

Wikipedia, Rimonabant, <http://en.wikipedia.org/wiki/Rimonabant>, downloaded 1/22/2009, reports: "Rimonabant reduced resumption of cocaine-seeking responses triggered by two of the three most common triggers of relapse in humans, priming and cues. It may also reduce ethanol- and opiate-seeking behavior." Wikipedia confirms the deleterious side effects:

> Shortly after market introduction, press reports and independent studies suggest that side-effects occur stronger and more commonly than shown by the manufacturer in their clinical studies. Reports of severe depression are frequent. This is deemed to result from the drug's being active in the central nervous system, an area of human physiology so complex that the effects of a drug are extremely difficult to predict or anticipate.
>
> Because the drug has the opposite effects of cannabinoid receptor agonists such as tetrahydrocannabinol (THC, one of the substances found in marijuana), which is neuroprotective against excitotoxicity, it can be

> theorized that Rimonabant promotes the development of neurodegenerative diseases of the central nervous system such as Multiple sclerosis, Alzheimer's disease, Amyotrophic lateral sclerosis, Parkinson's disease, and Huntington's disease in persons that are susceptible. The reported development of previously clinically-silent multiple sclerosis in one patient taking Rimonabant suggests that any patients with an underlying neurological condition should not take Rimonabant, given the neuroprotective role of the endocannabinoid system in many experimental paradigms of neurological disease.
>
> On 15 June 2007, BBC News reported that a committee advising the that [*sic*] US FDA had voted not to recommend the drug's approval because of concerns over suicidality, depression, and other related side-effects associated with use of the drug.

Ability of a CB1 modulator to effectively treat all conditions encompassed by the claims remains open to further study and proof.

5. **Working Examples:** Applicants do not provide highly predictive competent evidence or recognized tests of all recited conditions the claims encompass. Applicants do not provide competent evidence that the instantly disclosed tests are highly predictive for all uses covered embraced by claim language for all intended hosts.

6. **Skill of those in the art:** Koroneos and Wikipedia call into question treatment with the claimed methods and confirm the need for additional research.

7. **Quantity of experimentation needed to make or use the invention.** Based on the disclosure's content, one skilled in the pharmaceutical arts would have an undue burden to use the invention, since the disclosure gives the skilled artisan inadequate guidance regarding pharmaceutical use, for reasons explained above. The state of the art, as discussed in the articles above, indicates the requirement for undue experimentation. The ability of a CB1 modulator that treats all conditions construed by the claims remains open to further study and proof.

See MPEP 2164.01(a), discussed *supra*, justifying the conclusion of lack of enablement commensurate with the claim. Undue experimentation will be required to practice Applicants' invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 8, 10-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1:

- The recitation for any variable of "a saturated or partially unsaturated 5-to-8-membered heterocyclic group containing one or more … nitrogen" (or words to that effect) construes compounds in which the valency of nitrogen is unsatisfied.
- When "Y is absent," two separate unconnected moieties of the intended compound of Formula I are construed. The phrase -- Y is a single bond -- is suggested.
- The phrase "C1-3 acyl" fails to particularly point out and distinctly claim the intended subject matter. An acyl group is any functional group derived by the removal of one or more hydroxyl groups from any oxoacid, such as a carboxylic acid, sulfonic acid, phosphonic acid and unidentified others.

Claim 10:

It is not possible to determine what is intended by treatment of extended abuse, addiction and/or relapse indications. Abuse may refer to physical, substance and

sexual abuse, all of which require extremely different treatment forms. The term "addiction" is used in many contexts to describe any obsession, compulsion, or excessive or psychological dependence, e.g., drug addiction, crime, alcohol, tobacco, compulsive overeating, sex, problem gambling, computer addiction, pornography, etc. Relapse indications include return of disease signs and symptoms after a patient has enjoyed remission. For example, after treatment a patient with colon cancer went into remission with no sign or symptom of the tumor, remained in remission for years, but then suffered a relapse and had to be treated once again for colon cancer.

Claim 13:

- The phrase "coupling agent" fails to particularly point out and distinctly claim intended subject matter. It may be variously defined, e.g., material used to protect fiberglass laminates from water absorption effects; chemical substance capable of reacting with both reinforcement and resin matrix of composite material; agent used to provide a stable bond between otherwise nonbonding, incompatible surfaces, etc.
- The term "base" fails to particularly point out and distinctly claim the intended subject matter. It is inclusive of many compounds that may be variously defined:
    - **Arrhenius base**: a substance that increases the concentration of hydroxide ions when dissolved in water. This definition limits bases to substances that can dissolve in water.
    - **Brønsted-Lowry base**: a proton acceptor.
    - **Lewis base**: an electron-pair donor.

- The phrase “inert solvent,” “inert atmosphere" fail to particularly point out and distinctly claim the intended subject matter; they fail to define the substances and conditions to which they must be inert.
- The term “catalyst” fails to particularly point out and distinctly claim the intended subject matter; it encompasses any undefined substance that initiates or accelerates a chemical reaction without itself being affected.
- The terms “de-protecting” and “protected" fail to particularly point out and distinctly claim the intended subject matter; they fail to define the intended groups that are protected, the groups that provide the protection and the reagents and/or condition required from such de-protection.

Objected Claim – Allowable Subject Matter

Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Following is an examiner’s statement of reasons for indication of allowable subject matter.

Berggren, et al., US Pat. No 7,342,019, issued Mar. 11, 2008 describes substituted 5,6-diaryl-pyrazine-2-amide compounds. However, claim 6 is directed to 5,6-diaryl-pyrazine compounds with a particular substitution pattern which is neither anticipated nor rendered obvious by Berggren. In addition, none of the prior art of record anticipates or renders obvious the compounds of claim 6, whether taken individually or in any combination.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CECILIA M. JAISLE, J.D. whose telephone number is (571)272-9931. The examiner can normally be reached on Monday through Friday; 8:30 am through 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CECILIA M. JAISLE

1/19/2009

/James O. Wilson/

Supervisory Patent Examiner, Art Unit 1624